REMARKS

Claims 1-10 and 17-29 were at issue. Claims 1-10 and 17-25 were rejected. Claims 26-29 were withdrawn from consideration by the Examiner. The Examiner made the following rejections:

(1) The Examiner objects to claims 26-29 as being directed to a non-elected invention.

(2) Claim 1 and 17 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements / steps. Claims 2-10 and 18-25 are rejected as being dependent on indefinite base claims (e.g. Claims 1 and 17).

(3) Claims 1 and 17 are rejected under 35 U.S.C. 112 (first paragraph).

Applicants believe the present amendments and the following remarks traverse the Examiner's rejection of the claims. These remarks are presented in the same order as they appear above.

1. Claims 26-29 Are Within The Scope Of The Original Election

On November 27, 2000, the Examiner restricted the claims in the application as filed into three groups: Group I (Claims 1-10), Group II (Claims 11-15), and Group III (Claim 16). On December 6, 2000 the Applicants elected Group I (Claims 1-10) without traverse. In their "Response To Office Action Mailed December 15, 2000" the Applicants added new claims (e.g. 17 - 29) to the pending application. Subsequently, the Examiner (in the Office Action mailed August 13, 2001) summarily withdrew pending claims 26 - 29 from consideration. The Examiner stated that, "claims 26-29 [are] withdrawn from consideration as being directed to a non-elected invention."[1] In this regard the Examiner has, for a second time, restricted the claims in the pending application. The Applicants object.

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[1] Office Action mailed August 13, 2001, p. 2.

The Examiner is reminded that restriction is *only* proper if it can be shown that: (1) the claims belong to separate classifications; (2) a different field of search would be required; or (3) the claims have a separate status in the art (*e.g.*, as shown by citing patents that are evidence of such separate status or by showing a separate field of search) (MPEP 808.02). One of these three criteria *must* be established to support a restriction. Applicants assert that the Examiner *has not established any of these criteria* in support of the *de facto* restriction of pending claims 26 - 29.

The Examiner does not meet the first criteria for the restriction as the Examiner fails to enumerate, with specificity, which classes and subclasses would need be searched.

Similarly, the second criteria is not satisfied in view of the Examiner's failure to specifically cite evidence which suggests that a different field of search would be required to examine the claims in question. Therefore, the Examiner has made no showing (beyond bald conclusion) that the search and examination of *all pending claims* would be unduly burdensome.

Finally, the Examiner does not meet the third criteria given that the Examiner has, once again, not provided any evidence to support the argument that the pending claim set have a separate status in the art.

However, in order to advance their business interests (and without acquiescing to the Examiner's arguments) the Applicants have canceled claims 26 - 29 while reserving the right to prosecute the same, or similar, claims in subsequently filed applications.

2. The Claims Are Definite

Once again, the Examiner is reminded that "[c]laims of a patent application *are to be construed in the light of the specification* and the understanding thereof by those skilled in that art to whom they are addressed'." *Application of Salem*, 553 F.2d 676, 683, 193 USPQ 513 (CCPA 1977) (quoting *In re Myers*, 410 F.2d 420, 425 (CCPA 1969) with emphasis added in *Salem*). Furthermore, "[i]f the claims, read in the light of the specifications, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the courts can demand no more." *Georgia-Pacific Corp. v. United States Plywood Corp.*, 258 F.2d 124, 136, 118 USPQ 122, 132 (2d Cir.), *cert. denied*, 358 U.S. 884 (1958).

In view of the well settled case law cited above, Applicants do not agree that, "[i]t is not clear from the claim what exactly is meant by conditions for detection of demylenating disease".[2] Moreover, Applicants do not agree that independent Claim 1 and 17 are, "incomplete for omitting essential steps, such omissions amounting to a gap between the steps".[3] The specification of the application as filed provides numerous examples wherein the Applicants use the binding (or lack thereof) of iron binding proteins to a tissue sample as a means to detect, in a given sample, pathologies consistent with demyelinating diseases.

Indeed, as previously noted, the Applicants use *the lack* of ferritin binding observed in CNS lesions and periplaque margins as a means to detect demyelinating disease. While it is not intended that the present invention be limited to any one iron binding protein or binding mechanism, in one embodiment the Applicants teach that,

> "ferritin binding is absent within the lesion itself which suggests ferritin is not binding to microglia or astrocytes; the two other types of glial cells found in white matter and which heavily populate the lesion."[4]

* * *

> "[t]herefore the present invention contemplates assay systems which are based on the differential binding of ferritin in normal brains and the brains of persons afflicted with MS. In a preferred embodiment, immunocytochemical methods are used identify demyelinated lesions in the brain (consistent with a finding of MS) which substantially fail to bind ferritin."[5]

Conversely, the Applicants use the binding of transferrin in periplaque regions as another means to detect demyelinating disease. Specifically, the Applicants teach that,

> "the normal distributions of transferrin and ferritin binding sites are altered in and around plaques from periventricular white matter isolated from multiple sclerotic (MS) brains. In direct contrast to ferritin binding, transferrin binding in the MS tissue can be seen in white matter periplaque regions and to varying degrees within the lesion itself."[6]

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[2] *Id.* at p. 3.

[3] *Id.*

[4] Application as filed, p. 8, ll. 14-16.

[5] *Id.* at p. 8, ll. 22-25.

[6] *Id* at, p. 8, ll. 6-10.

The Applicants teach the relative binding of iron binding proteins as an index to differentially detect pathologies consistent with demyelinating disease in a sample from a human suspected of having a demyelinating disease. That is to say, the specification correlates the degree of binding between a human tissue sample and a specific iron binding protein to the detection of a demyelinating disease in a tissue. The Applicants, therefore, provide a detailed teaching in the specification for various means to detect demylenating disease.

The Applicants, however, are under no obligation[7] to import (from the specification) these detailed recitation of, "differential binding, relative binding, [and] degree of binding. . ."[8] (of iron binding proteins) into the invention as claimed. Indeed, the Examiner is reminded that,

> "it is not the normal function of a claim to disclose the invention, but to point out the features of novelty in the invention as disclosed in the specification and drawing of the application." *Bocciarelli v. Huffman*, 109 USPQ 385, 388 (C.C.P.A. 1956).

Moreover, the law is clear that, "[i]t is entirely proper to use the specification to interpret what the patentee meant by a word or phrase in the claim." *E.I. du Pont de Nemours & Co. v. Phillips Petroleum Co.*, 849 F.2d 1430, 1433 (Fed. Cir. 1988). The Applicants pending claims recite an integrated and complete set of steps in methods for the detection of demylenating disease that, when read in view of the specification, provide all essential steps to practice the invention as claimed.

However, in order to advance their business interests and without acquiescing to the Examiner's argument, while expressly reserving the right to prosecute the claims as originally filed (or claims similar thereto), Applicants have amended claims 1 and 17. Specifically, Applicants have reorganized theses claims such that the methods now focus on the detection of altered distributions of protein binding sites. This amended language is supported by the specification[9] and, therefore, the instant amendment add no new matter to the pending application. Therefore, the claims (read in view of the specification) particularly point out

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[7] In order to satisfy 35 U.S.C. § 112 (second paragraph).

[8] Steps alleged, by the Examiner, as essential to the invention as claimed. See, Office Action mailed August 13, 2001, p. 3.

[9] See, for example, page 8, ll. 1-11 of the application as filed.

and distinctly claim all essential steps (and the interconnection between these steps) in the methods which the Applicants view as their invention. The Examiner, therefore, is respectfully requested to withdraw the pending rejections under 35 U.S.C. § 112 (second paragraph).

3. The Claims Are Enabled

A. The Examiner Fails To Make A *Prima Facie* Case.

The Examiner rejects Claims 1 and 17 under 35 U.S.C. 112, first paragraph. Specifically, the Examiner alleges the specification does not allow any person skilled in the art to, "use the invention commensurate in scope with these claims."[10] The Examiner is reminded that, "it is incumbent upon the Patent Office, whenever a rejection on [the basis of lack of enablement] is made, to explain why it doubts the truth or accuracy of any statement in supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement." *In re Marzocchi*, 169 USPQ 367, 370 (CCPA 1971).

In view of *In re Marzocchi*, Applicants submit that the Examiner fails to provide adequate explanation, evidence, or reasoning as to why the Applicants' specification fails to enable the scope of the invention as claimed. Instead, the Examiner summarily applies an 'undue experimentation' stamp upon the case (while discounting the adequacy of the teachings in the Application as filed) to improperly advance a *prima facie* case.

B. The Specification Enables The Claims As Filed

The Examiner asserts the,

> "specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with theses claims. . .[i]t would require undue experimentation for one skilled in the art to practice the invention as currently claimed using for example fluid samples, or any other samples of human tissue, except samples of the brain tissue."[11]

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[10] Office Action Mailed August 13, 2001, page 4.

[11] *Id.*

The Examiner is reminded that, in an undue experimentation analysis, "[t]he key word is 'undue' not 'experimentation.'" *In re Angstadt and Griffin*, 190 USPQ 214, 219 (CCPA 1976). Indeed, "a considerable amount of experimentation is permissible . . . if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed . . . ." *Ex parte Jackson*, 217 USPQ 804, 807 (Bd. App. 1982); *In re Wands*, 8 USPQ 2d 1400, 1404 (CAFC 1988). Therefore, the Examiner's case for undue experimentation should be based on an evaluation of Applicants' teaching and is not satisfied by a vague reference to the problems encountered by others in the Art.

The Examiner's observation that,

> "the state of the art of protein binding using antibodies or any other binding substances is not predictable enough to extrapolate the data collected from the experiments collected from tissue slices to predict the success of the same technique (method) when working with liquid samples"[12]

is conclusory. That is to say, the Examiner fails to cite any reference which substantiates the alleged "unpredictability" *vis-a-vis* the invention as claimed.

Similarly, the "total absence of working examples"[13] (for fluid samples) is insufficient, by itself, to support a rejection under 35 U.S.C. § 112 (first paragraph). Indeed, the Examiner is reminded that

> "[c]ompliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, does not turn on whether an example is disclosed. . .[t]he specification need not contain an example if the invention is otherwise disclosed in such manner that one of skill in the art will be able to practice it without an undue amount of experimentation." See, MPEP 2164.02.

Applicants teach that the, "present invention also contemplates a method for the detection of a demyelinating disease comprising providing a fluid sample from a human suspected of having a demyelinating disease, reacting said fluid sample with human ferritin binding protein, and detecting the binding of antibodies within said fluid sample to said

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[12] *Id.* at page 5.

[13] *Id.*

ferritin binding protein."[14] Furthermore, the Applicants provide a specific definition for 'fluid sample' wherein,

> "the term 'fluid sample' refers to samples taken from whole blood, blood plasma, blood serum, extravascular fluid, cerebral spinal fluid, lymph, interstitial fluid, pleural fluid, prostatic fluid, sucular fluid, ventricular fluid, synovial fluid, and stool."[15]

In addition Applicants describe numerous immuno-reactive scenarios as background for embodiments of the present invention which are directed to the detection of antibodies against brain ferritin binding protein in the brain as a diagnostic method for multiple sclerosis.[16]

In view of the teachings outlined above, Applicants submit that the claims as filed are compliant with the enabelment requirement of 35 U.S.C. 112, first paragraph. However, in order to advance their business interests and without acquiescing to the Examiner's argument, while expressly reserving the right to prosecute the claims as originally filed (or claims similar thereto), Applicants have amended claims 1, 2, 17 and 18. Specifically, Applicants have amended the claimed methods such that they are now directed to a "tissue sample".

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[14] Application as filed, page 3, ll. 16-19.

[15] *Id.* at page 6, ll. 2-4.

[16] See, for example, Application as filed pp. 8-18.

CONCLUSION

The Applicants believe that the arguments and claim amendments set forth above traverse the Examiner's rejections and, therefore, request that these grounds for rejection be withdrawn for the reasons set above. Should the Examiner believe that a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned collect at 617.252.3353.

Dated: November 13, 2001

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APPENDIX I
MARKED-UP VERSION OF REWRITTEN CLAIMS
PURSUANT TO 37 CFR § 1.121 (c)(1)(ii)

1. A method for the detection of [a demyelinating disease] altered distributions of protein binding sites comprising:

a) providing: i) a tissue sample from a human suspected of having a demyelinating disease, and ii) iron binding protein;

b) reacting said tissue sample with said iron binding protein in vitro; and

c) measuring the extent of binding of said iron binding protein to said tissue sample, under conditions such that [a demyelinating disease is detected] altered distributions of iron binding protein sites are detectable.

2. The method of Claim 1, wherein said tissue sample is brain tissue.

17. A method for the detection of [a demyelinating disease] altered distributions of protein binding sites comprising:

a) providing: i) a tissue sample from a human suspected of having a demyelinating disease, and ii) iron binding protein wherein said iron binding protein is linked to a detectable marker;

b) reacting said tissue sample with said iron binding protein in vitro; and

c) measuring the extent of binding of said iron binding protein to said tissue sample, under conditions such that [a demyelinating disease is detected] altered distributions of iron binding protein sites are detectable.

18. The method of Claim 17, wherein said tissue sample is brain tissue.

APPENDIX II
CLEAN VERSION OF THE ENTIRE SET OF PENDING CLAIMS PURSUANT TO 37 CFR § 1.121 (c)(3)

1. A method for the detection of altered distributions of protein binding sites comprising:

   a) providing: i) a tissue sample from a human suspected of having a demyelinating disease, and ii) iron binding protein;

   b) reacting said tissue sample with said iron binding protein in vitro; and

   c) measuring the extent of binding of said iron binding protein to said tissue sample, under conditions such that altered distributions of iron binding protein sites are detectable.

2. The method of Claim 1, wherein said tissue sample is brain tissue.

3. The method of Claim 2, wherein said brain tissue is collected *via* surgical biopsy.

4. The method of Claim 1, wherein said iron binding protein is ferritin.

5. The method of Claim 4, wherein said ferritin is native.

6. The method of Claim 4, wherein said ferritin is recombinant.

7. The method of Claim 4, wherein said ferritin is linked to a detectable marker.

8. The method of Claim 7, wherein said marker is selected from the group consisting of radioisotope and fluorescent dye.

9. The method of Claim 8, wherein said radioisotope is ^{125}I.

10. The method of Claim 1, wherein said measuring is performed with a technique selected from the group of autoradiography and immunofluorescence.

17. A method for the detection of altered distributions of protein binding sites comprising:

a) providing: i) a tissue sample from a human suspected of having a demyelinating disease, and ii) iron binding protein wherein said iron binding protein is linked to a detectable marker;

b) reacting said tissue sample with said iron binding protein in vitro; and

c) measuring the extent of binding of said iron binding protein to said tissue sample, under conditions such that altered distributions of iron binding protein sites are detectable.

18. The method of Claim 17, wherein said tissue sample is brain tissue.

19. The method of Claim 18, wherein said brain tissue is collected *via* surgical biopsy.

20. The method of Claim 17, wherein said iron binding protein is ferritin.

21. The method of Claim 20, wherein said ferritin is native.

22. The method of Claim 20, wherein said ferritin is recombinant.

23. The method of Claim 17, wherein said marker is selected from the group consisting of radioisotope and florescent dye.

24. The method of Claim 23, wherein said radioisotope is ^{125}I.

25. The method of Claim 17, wherein said measuring is performed with a technique selected from the group of autoradiography and immunofluorescence.